

## P/ NT COOPERATION TREA

PCT

## NOTIFICATION OF ELECTION

(PCT Rule 61.2)

From the INTERNATIONAL BUREAU

To:

Commissioner  
 US Department of Commerce  
 United States Patent and Trademark  
 Office, PCT  
 2011 South Clark Place Room  
 CP2/5C24  
 Arlington, VA 22202  
 ETATS-UNIS D'AMERIQUE

in its capacity as elected Office

<b>Date of mailing (day/month/year)</b> 31 October 2000 (31.10.00)	<b>Applicant's or agent's file reference</b> P020968WO
<b>International application No.</b> PCT/IB00/00219	<b>Priority date (day/month/year)</b> 22 February 1999 (22.02.99)
<b>International filing date (day/month/year)</b> 22 February 2000 (22.02.00)	<b>Applicant</b> GEBAUER, Fatima et al

1. The designated Office is hereby notified of its election made:

☒ in the demand filed with the International Preliminary Examining Authority on:

20 September 2000 (20.09.00)

☐ in a notice effecting later election filed with the International Bureau on:2. The election ☒ was☐ was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland  Facsimile No.: (41-22) 740.14.35	Authorized officer  Juan Cruz  Telephone No.: (41-22) 338.83.38
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# PATENT COOPERATION TREATY

From the  
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

PCT

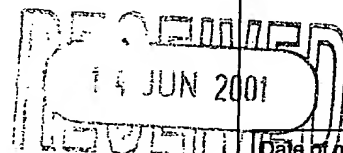
To:

HALLYBONE, Huw George  
CARPMAELS & RANSFORD  
43 Bloomsbury Square  
London WC1A 2RA  
GRANDE BRETAGNE

## NOTIFICATION OF TRANSMITTAL OF THE INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Rule 71.1)

*AKG*



Date of mailing

(day/month/year)

12.06.2001

Applicant's or agent's file reference

P020968WO-HGH

### IMPORTANT NOTIFICATION

International application No.

PCT/IB00/00219

International filing date (day/month/year)

22/02/2000

Priority date (day/month/year)

22/02/1999

Applicant

EUROPEAN MOLECULAR BIOLOGY LABORATORY et al.

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international application.
2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.
3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.

#### 4. REMINDER

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices) (Article 39(1)) (see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

Name and mailing address of the IPEA/

European Patent Office  
D-80298 Munich  
Tel. +49 89 2399 - 0 Tx: 523656 epmu d  
Fax: +49 89 2399 - 4465

Authorized officer

Neumann, M

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PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference P020968WO-HGH	<b>FOR FURTHER ACTION</b> See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/IB00/00219	International filing date (day/month/year) 22/02/2000	Priority date (day/month/year) 22/02/1999
International Patent Classification (IPC) or national classification and IPC C12N15/09		
Applicant EUROPEAN MOLECULAR BIOLOGY LABORATORY et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.



2. This REPORT consists of a total of 7 sheets, including this cover sheet.

- ☐ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☒ Certain observations on the international application

Date of submission of the demand  20/09/2000	Date of completion of this report  12.06.2001
Name and mailing address of the international preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer  Barnas, C  Telephone No. +49 89 2399 7469 

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT**

International application No. PCT/IB00/00219

**I. Basis of the report**

1. With regard to the **elements** of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17)*):  
**Description, pages:**

1-22 as originally filed

**Claims, No.:**

1-44 as originally filed

**Drawings, sheets:**

1-13 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).  
☐ the language of publication of the international application (under Rule 48.3(b)).  
☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.  
☐ filed together with the international application in computer readable form.  
☐ furnished subsequently to this Authority in written form.  
☐ furnished subsequently to this Authority in computer readable form.  
☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.  
☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:  
☐ the claims, Nos.:

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT**

International application No. PCT/IB00/00219

☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

*(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)*

6. Additional observations, if necessary:

**III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application.

☒ claims Nos. 16-39, 40 (part), 41-44.

because:

☐ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination (*specify*):

☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☒ no international search report has been established for the said claims Nos. 16-39, 40 (part), 41-44.

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

☐ the written form has not been furnished or does not comply with the standard.

☐ the computer readable form has not been furnished or does not comply with the standard.

**V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

1. Statement

Novelty (N)

Yes: Claims 4, 7-12, 14, 15, 40

**INTERNATIONAL PRELIMINARY  
EXAMINATION REPORT**

International application No. PCT/IB00/00219

	No:	Claims	1-3, 5, 6, 13
Inventive step (IS)	Yes:	Claims	8-10, 15
	No:	Claims	4, 7, 11, 12, 14, 40
Industrial applicability (IA)	Yes:	Claims	1-15, 40
	No:	Claims	

2. Citations and explanations  
**see separate sheet**

**VIII. Certain observations on the international application**

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:  
**see separate sheet**

**Re Item III**

**Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

Claims 28-36, 39, 42-44 refer to subject matter which has not been searched. Said claims can, therefore, also not be subjected to examination. Claim 40 can only be examined as far as referring to claims 1-15.

**Re Item V**

**Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

- D1: SCOTT M P ET AL.: 'Cell-free protein synthesis in lysates of *Drosophila melanogaster* cells' BIOCHEMISTRY, vol. 18, no. 8, 1979, pages 1588-1594, XP002140264 cited in the application
- D2: IIZUKA N ET AL.: 'Cap-dependent and cap-independent translation by internal initiation of mRNAs in cell extracts prepared from *Saccharomyces cerevisiae*' MOLECULAR AND CELLULAR BIOLOGY, vol. 14, no. 11, November 1994 (1994- 11), pages 7322-7330, XP000914650 cited in the application

**1. Art. 33(2) PCT, Novelty**

1.1. D1 (p. 1591, Fig.1D) discloses methods for in vitro translation wherein a mRNA is incubated for 45 min. with a reaction mix containing both a cell extract from rat liver and Schneider L-2 *Drosophila* cells or with a *Drosophila* embryo cell extract. Said mRNA has been extracted from cells and, therefore, contains both a 5'cap and a 3'polyA (see p. 1588, right column, "RNA and Protein extraction").

In addition D1 discloses in vitro translation of said mRNA in the reaction mix containing both a cell extract from rat liver and Schneider L-2 *Drosophila* cells with an incubation time of 60 min (see p. 1591, Fig. 1).

The present application shows in Fig. 1. that incubating a mRNA with 5'cap and 3'polyA in the *Drosophila* embryo cell extract of D1 for longer than 45 min. using in vitro translation conditions as described in D1 results in amounts of protein as described in claim 1 (compare extract Scott, conditions Scott 45 min. and extract Scott, conditions Scott

90 min in Fig. 1 of the application). Thus, the method shown in Fig. 1D of D1 with an incubation time of 60 min., using cell extracts from rat liver and Schneider L-2 Drosophila cells, is also regarded as leading to protein amounts as described in claim 1. Said method of D1 is, therefore, novelty destroying for **claims 1-3, 5 and 6**.

1.2. The in vitro reactions disclosed in D1 comprise all of the substances listed in claim 13 (see p.1589, left column, paragraphs 8 and 9 and p. 1590 Table II). **Claim 13** is, therefore, not new.

## **2. Art. 33(3) PCT, Inventive Step**

2.1. D1 represents the closest prior art for the present application. Said document discloses that longer incubation times result in increased amounts of translation products (see Fig. 1D and p. 1590, right column, paragraph 2, Ins. 6-8). These results, would, therefore, prompt the skilled person to incubate a mRNA with the Drosophila embryo cell extract of D1 for more than one hour. The skilled person would, therefore, arrive at a method as shown in Fig. 1 of the present application (extract Scott, conditions Scott 90 min.) without the exercise of inventive skill. **Claims 7 and 14** are, therefore, not inventive.

2.2. The use of human cell extracts for in vitro translation is known in the prior art (see D2, Fig. 4). The skilled person would, therefore, regard it as a design procedure to apply the method disclosed in D1 with incubation times of at least one hour (see p. 1590, right column, paragraph 2, Ins. 6-8) using human cell extracts. **Claim 4** is, therefore, not inventive.

2.3. The present application does not disclose any specific effect which results from the use of Drosophila ovary cell extracts instead of the extracts shown in D1. The use of such extracts represents, therefore, arbitrary modifications of the method of claim 1 which do not include an inventive step. **Claims 11 and 12** are, therefore, not inventive.

2.4. The identification of molecules that increase or decrease the amount of a produced translation product is a routine procedure which the skilled person would apply without the exercise of inventive skill. (see D1, p. 1590, Table II). **Claim 40** is, therefore, not inventive.



**3. Additional Observations**

D1 is considered as the closest prior art for the present application. The difference to said document is the provision of a further method for the in vitro translation of a ribonucleic acid template. The cited prior art does not contain any indication that would prompt the skilled person to dechorionate *Drosophila* embryos as described in claim 8 or to incubate at 25°C, as described in claim 15. Claims 8-10 and 15 seem, therefore, inventive.

**Re Item VIII**

**Certain observations on the international application**

1. According to the description of the present application Fig. 12A and 12B should show the same results for Cap and Cap-pA transcripts. The results shown in Fig. 12A and 12B for said transcripts, however, differ from each other. This discrepancy cannot be understood from the technical point of view.
2. The terms used in Fig. 13 are not explained in the description. Thus, said figure cannot be interpreted in a meaningful way.

# PATENT COOPERATION TREATY

✓ HRC

From the  
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

PCT

HGH

To:

HALLYBONE, Huw George  
CARPMAELS & RANSFORD  
43 Bloomsbury Square  
London WC1A 2RA  
GRANDE BRETAGNE

DJ

## NOTIFICATION OF RECEIPT OF DEMAND BY COMPETENT INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

(PCT Rules 59.3(e) and 61.1(b), first sentence  
and Administrative Instructions, Section 601(a))

Date of mailing  
(day/month/year)

05.10.00

Applicant's or agent's file reference  
P020968WO-HGH

### IMPORTANT NOTIFICATION

International application No.

PCT/IB 00/00219

International filing date (day/month/year)

22/02/2000

Priority date (day/month/year)

22/02/1999

Applicant

EUROPEAN MOLECULAR BIOLOGY LABORATORY et al.

1. The applicant is hereby notified that this International Preliminary Examining Authority considers the following date as the date of receipt of the demand for international preliminary examination of the international application:

20/09/2000

2. This date of receipt is:

- ☒ the actual date of receipt of the demand by this Authority (Rule 61.1(b)).
- ☐ the actual date of receipt of the demand on behalf of this Authority (Rule 59.3(e)).
- ☐ the date on which this Authority has, in response to the invitation to correct defects in the demand (Form PCT/IPEA/404), received the required corrections.

3. ☐ **ATTENTION:** That date of receipt is **AFTER** the expiration of 19 months from the priority date. Consequently, the election(s) made in the demand does (do) not have the effect of postponing the entry into the national phase until 30 months from the priority date (or later in some Offices) (Article 39(1)). Therefore, the acts for entry into the national phase must be performed within 20 months from the priority date (or later in some Offices) (Article 22). For details, see the *PCT Applicant's Guide*, Volume II.

- ☐ (If applicable) This notification confirms the information given by telephone, facsimile transmission or in person on:

4. Only where paragraph 3 applies, a copy of this notification has been sent to the International Bureau.

Name and mailing address of the IPEA/

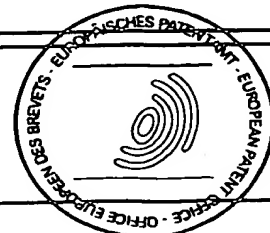


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Authorized officer

MORENO R A

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# PATENT COOPERATION TREATY

✓ HRC

DUE 26.4.01

From the:  
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To:

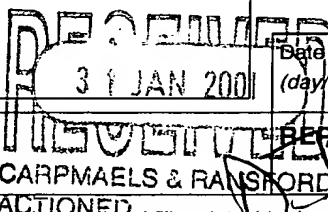
HALLYBONE, Huw George  
CARPMAELS & RANSFORD  
43 Bloomsbury Square  
London WC1A 2RA  
GRANDE BRETAGNE

PCT

HRC

WRITTEN OPINION

(PCT Rule 66)

		Date of mailing (day/month/year)	26.01.2001
Applicant's or agent's file reference P020968WO-HGH		<b>REPLY DUE</b>	within 3 month(s) from the above date of mailing
International application No. PCT/IB00/00219	International filing date (day/month/year) 22/02/2000	Priority date (day/month/year) 22/02/1999	
International Patent Classification (IPC) or both national classification and IPC C12N15/09			
Applicant EUROPEAN MOLECULAR BIOLOGY LABORATORY et al.			

1. This written opinion is the **first** drawn up by this International Preliminary Examining Authority.
2. This opinion contains indications relating to the following items:
  - I    ☒ Basis of the opinion
  - II   ☐ Priority
  - III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
  - IV   ☐ Lack of unity of invention
  - V    ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
  - VI   ☐ Certain document cited
  - VII ☐ Certain defects in the international application
  - VIII ☒ Certain observations on the international application

3. The applicant is hereby **invited to reply** to this opinion.


**When?**      See the time limit indicated above. The applicant may, before the expiration of that time limit, request this Authority to grant an extension, see Rule 66.2(d).

**How?**        By submitting a written reply, accompanied, where appropriate, by amendments, according to Rule 66.3. For the form and the language of the amendments, see Rules 66.8 and 66.9.

**Also:**        For an additional opportunity to submit amendments, see Rule 66.4.  
For the examiner's obligation to consider amendments and/or arguments, see Rule 66.4 bis.  
For an informal communication with the examiner, see Rule 66.6.

**If no reply is filed**, the international preliminary examination report will be established on the basis of this opinion.

4. The final date by which the international preliminary examination report must be established according to Rule 69.2 is: **22/06/2001**.

Name and mailing address of the international preliminary examining authority:   European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized officer / Examiner  Barnas, C  Formalities officer (incl. extension of time limits) Zoglauer, H Telephone No. +49 89 2399 8051
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**I. Basis of the opinion**

1. This opinion has been drawn on the basis of (*substitute sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this opinion as "originally filed".*):

**Description, pages:**

1-22 as originally filed

**Claims, No.:**

1-44 as originally filed

**Drawings, sheets:**

1-13 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:

☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

*(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)*

6. Additional observations, if necessary:

**III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been and will not be examined in respect of:

- ☐ the entire international application,  
☒ claims Nos. 16-39, 40 (part), 41-44,

because:

- ☐ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination (*specify*):
- ☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):
- ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.
- ☒ no international search report has been established for the said claims Nos. 16-39, 40 (part), 41-44.

2. A written opinion cannot be drawn due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

- ☐ the written form has not been furnished or does not comply with the standard.  
☐ the computer readable form has not been furnished or does not comply with the standard.

**V. Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

1. Statement  
 Novelty (N) Claims 1-3, 5, 6, 13 (NO)  
 Inventive step (IS) Claims 4, 7, 11, 12, 14, 40 (NO)

Industrial applicability (IA)      Claims

2. Citations and explanations  
**see separate sheet**

**VIII. Certain observations on the international application**

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:  
**see separate sheet**

**Re Item III**

**Non-establishment of opinion with regard to novelty, inventive step and industrial applicability**

Claims 28-36, 39, 42-44 refer to subject matter which has not been searched. Said claims can, therefore, also not been subjected to examination. Claim 40 can only be examined as far as referring to claims 1-15.

**Re Item V**

**Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

- D1: SCOTT M P ET AL.: 'Cell-free protein synthesis in lysates of *Drosophila melanogaster* cells' *BIOCHEMISTRY*, vol. 18, no. 8, 1979, pages 1588-1594, XP002140264 cited in the application
- D2: IIZUKA N ET AL.: 'Cap-dependent and cap-independent translation by internal initiation of mRNAs in cell extracts prepared from *Saccharomyces cerevisiae*' *MOLECULAR AND CELLULAR BIOLOGY*, vol. 14, no. 11, November 1994 (1994-11), pages 7322-7330, XP000914650 cited in the application

**1. Art. 33(2) PCT, Novelty**

1.1. D1 (p. 1591, Fig.1D) discloses methods for in vitro translation wherein a mRNA is incubated for 45 min. with a reaction mix containing both a cell extract from rat liver and Schneider L-2 *Drosophila* cells or with a *Drosophila* embryo cell extract. Said mRNA has been extracted from cells and, therefore, contains both a 5'cap and a 3'polyA (see p. 1588, right column, "RNA and Protein extraction").

In addition D1 discloses in vitro translation of said mRNA in the reaction mix containing both a cell extract from rat liver and Schneider L-2 *Drosophila* cells with an incubation time of 60 min (see p. 1591, Fig. 1).

The present application shows in Fig. 1. that incubating a mRNA with 5'cap and 3'polyA in the *Drosophila* embryo cell extract of D1 for longer than 45 min. using in vitro translation conditions as described in D1 results in amounts of protein as described in

claim 1 (compare extract Scott, conditions Scott 45 min. and extract Scott, conditions Scott 90 min in Fig. 1 of the application). Thus, the method shown in Fig. 1D of D1 with an incubation time of 60 min., using cell extracts from rat liver and Schneider L-2 Drosophila cells, is also regarded as leading to protein amounts as described in claim 1. Said method of D1 is, therefore, novelty destroying for **claims 1-3, 5 and 6**.

1.2. The in vitro reactions disclosed in D1 comprise all of the substances listed in claim 13 (see p.1589, left column, paragraphs 8 and 9 and p. 1590 Table II). **Claim 13** is, therefore, not new.

## **2. Art. 33(3) PCT, Inventive Step**

2.1. D1 represents the closest prior art for the present application. Said document discloses that longer incubation times result in increased amounts of translation products (see Fig. 1D and p. 1590, right column, paragraph 2, Ins. 6-8). These results, would, therefore, prompt the skilled person to incubate a mRNA with the Drosophila embryo cell extract of D1 for more than one hour. The skilled person would, therefore, arrive at a method as shown in Fig. 1 of the present application (extract Scott, conditions Scott 90 min.) without the exercise of inventive skill. **Claims 7 and 14** are, therefore, not inventive.

2.2. The use of human cell extracts for in vitro translation is known in the prior art (see D2, Fig. 4). The skilled person would, therefore, regard it as a design procedure to apply the method disclosed in D1 with incubation times of at least one hour (see p. 1590, right column, paragraph 2, Ins. 6-8) using human cell extracts. **Claim 4** is, therefore, not inventive.

2.3. The present application does not disclose any specific effect which results from the use of Drosophila ovary cell extracts instead of the extracts shown in D1. The use of such extracts represents, therefore, arbitrary modifications of the method of claim 1 which do not include an inventive step. **Claims 11 and 12** are, therefore, not inventive.

2.4. The identification of molecules that increase or decrease the amount of a produced translation product is a routine procedure which the skilled person would apply without the exercise of inventive skill. (see D1, p. 1590, Table II). **Claim 40** is, therefore, not inventive.



**Re Item VIII**

**Certain observations on the international application**

According to the description of the present application Fig. 12A and 12B should show the same results for Cap and Cap-pA transcripts. The results shown in Fig. 12A and 12B for said transcripts, however, differ from each other. This discrepancy cannot be understood from the technical point of view.

The terms used in Fig. 13 are not explained in the description. Thus, said figure cannot be interpreted in a meaningful way.

*The applicant is requested to file new claims and/or explanations which take account of the above comments. The attention of the applicant is drawn to the fact that the application may not be amended in such a way that it contains subject-matter which extends beyond the content of the application as filed, Art. 34 (2) PCT. Therefore, the applicant is asked to indicate the basis of any amendments to the claims in the application documents originally filed.*

The demand must be filed directly with the competent International Preliminary Examining Authority or, if two or more Authorities are competent, with the one chosen by the applicant. The full name or two-letter code of that Authority may be indicated by the applicant on the line below:

IPEA/ EP

PCT

CHAPTER II

DEMAND

under Article 31 of the Patent Cooperation Treaty:  
The undersigned requests that the international application specified below be the subject of international preliminary examination according to the Patent Cooperation Treaty and hereby elects all eligible States (except where otherwise indicated).

For International Preliminary Examining Authority use only		
Identification of IPEA		Date of receipt of DEMAND
<b>Box No. I IDENTIFICATION OF THE INTERNATIONAL APPLICATION</b>		Applicant's or agent's file reference P020968WO:HG
International application No. PCT/IB00/00219	International filing date (day/month/year) 22.02.2000	(Earliest) Priority date (day/month/year) 22.02.1999
Title of invention TRANSLATION SYSTEM		
<b>Box No. II APPLICANT(S)</b>		
Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country.)  EUROPEAN MOLECULAR BIOLOGY LABORATORY P.O. BOX 10 22 09 MEYERHOFSTR. 1 69012 HEIDELBERG DE		Telephone No.:
		Facsimile No.:
		Teleprinter No.:
State (that is, country) of nationality: DE		State (that is, country) of residence: DE
Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country.)  GEBAUER, Fatima LERCHENSTRASSE 28 69251 GAIBERG DE		
State (that is, country) of nationality: ES		State (that is, country) of residence: DE
Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country.)  CORONA, Davide BRECHTELSTRASSE 8-10 69126 HEIDELBERG DE		
State (that is, country) of nationality: IT		State (that is, country) of residence: DE
<input checked="" type="checkbox"/> Further applicants are indicated on a continuation sheet.		

## Continuation of Box No. II APPLICANT(S)

*If none of the following sub-boxes is used, this sheet should not be included in the demand.*

Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country.)

BERGAMINI, Giovanna  
RÖMERSTR. 25  
69115 HEIDELBERG  
DE

State (that is, country) of nationality:

IT

State (that is, country) of residence:

DE

Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country.)

BECKER, Peter  
SALZSTR. 9  
82194 GRÖBENZELL  
DE

State (that is, country) of nationality:

DE

State (that is, country) of residence:

DE

Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country.)

HENTZE, Matthias  
MERIANSTR. 5  
69117 HEIDELBERG  
DE

State (that is, country) of nationality:

DE

State (that is, country) of residence:

DE

Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country.)

State (that is, country) of nationality:

State (that is, country) of residence:

☐

Further applicants are indicated on another continuation sheet.

**Box No. III AGENT OR COMMON REPRESENTATIVE; OR ADDRESS FOR CORRESPONDENCE**The following person is ☒ agent ☐ common representativeand ☒ has been appointed earlier and represents the applicant(s) also for international preliminary examination.☐ is hereby appointed and any earlier appointment of (an) agent(s)/common representative is hereby revoked.☐ is hereby appointed, specifically for the procedure before the International Preliminary Examining Authority, in addition to the agent(s)/common representative appointed earlier.Name and address: *(Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country.)*HALLYBONE, Huw George  
CARPMAELS & RANSFORD  
43 BLOOMSBURY SQUARE  
LONDON WC1A 2RA  
UNITED KINGDOM

Telephone No.:

020-7242 8692

Facsimile No.:

020-7405 4166

Teleprinter No.:

267209

☐ Address for correspondence: Mark this check-box where no agent or common representative is/has been appointed and the space above is used instead to indicate a special address to which correspondence should be sent.**Box No. IV BASIS FOR INTERNATIONAL PRELIMINARY EXAMINATION****Statement concerning amendments: \***

1. The applicant wishes the international preliminary examination to start on the basis of:

☒ the international application as originally filedthe description ☐ as originally filed☐ as amended under Article 34the claims ☐ as originally filed☐ as amended under Article 19 (together with any accompanying statement)☐ as amended under Article 34the drawings ☐ as originally filed☐ as amended under Article 342. ☐ The applicant wishes any amendment to the claims under Article 19 to be considered as reversed.3. ☐ The applicant wishes the start of the international preliminary examination to be postponed until the expiration of 20 months from the priority date unless the International Preliminary Examining Authority receives a copy of any amendments made under Article 19 or a notice from the applicant that he does not wish to make such amendments (Rule 69.1(d)). *(This check-box may be marked only where the time limit under Article 19 has not yet expired.)*

\* Where no check-box is marked, international preliminary examination will start on the basis of the international application as originally filed or, where a copy of amendments to the claims under Article 19 and/or amendments of the international application under Article 34 are received by the International Preliminary Examining Authority before it has begun to draw up a written opinion or the international preliminary examination report, as so amended.

Language for the purposes of international preliminary examination: ENGLISH☒ which is the language in which the international application was filed.☐ which is the language of a translation furnished for the purposes of international search.☐ which is the language of publication of the international application.☐ which is the language of the translation (to be) furnished for the purposes of international preliminary examination.**Box No. V ELECTION OF STATES**The applicant hereby elects all eligible States *(that is, all States which have been designated and which are bound by Chapter II of the PCT)*

excluding the following States which the applicant wishes not to elect:

**Box No. VI CHECK LIST**

The demand is accompanied by the following elements, in the language referred to in Box No. IV, for the purposes of international preliminary examination:

- |  |   |        |
|--|---|--------|
| 1. translation of international application                              | : | sheets |
| 2. amendments under Article 34   | : | sheets |
| 3. copy (or, where required, translation) of amendments under Article 19 | : | sheets |
| 4. copy (or, where required, translation) of statement under Article 19  | : | sheets |
| 5. letter  | : | sheets |
| 6. other ( <i>specify</i> )  | : | sheets |

## For International Preliminary Examining Authority use only

received	not received
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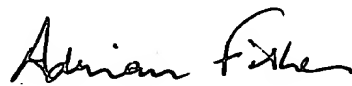

<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	<input type="checkbox"/>
<input type="checkbox"/>	<input type="checkbox"/>

The demand is also accompanied by the item(s) marked below:

- |  |   |
|--|---|
| 1. <input checked="" type="checkbox"/> fee calculation sheet                             | 4. <input type="checkbox"/> statement explaining lack of signature                                  |
| 2. <input type="checkbox"/> separate signed power of attorney                            | 5. <input type="checkbox"/> nucleotide and or amino acid sequence listing in computer readable form |
| 3. <input type="checkbox"/> copy of general power of attorney; reference number, if any: | 6. <input type="checkbox"/> other ( <i>specify</i> ):   |

**Box No. VII SIGNATURE OF APPLICANT, AGENT OR COMMON REPRESENTATIVE**

Next to each signature, indicate the name of the person signing and the capacity in which the person signs (if such capacity is not obvious from reading the demand).

 Fisher, Adrian John  
HALLYBONE, Huw George  


## For International Preliminary Examining Authority use only

1. Date of actual receipt of DEMAND:

2. Adjusted date of receipt of demand due to CORRECTIONS under Rule 60.1(b):

3. ☐ The date of receipt of the demand is AFTER the expiration of 19 months from the priority date and item 4 or 5, below, does not apply.

☐ The applicant has been informed accordingly.

4. ☐ The date of receipt of the demand is WITHIN the period of 19 months from the priority date as extended by virtue of Rule 80.5.

5. ☐ Although the date of receipt of the demand is after the expiration of 19 months from the priority date, the delay in arrival is EXCUSED pursuant to Rule 82.

## For International Bureau use only

Demand received from IPEA on:

## PATENT COOPERATION TREATY

✓ 429

PCT

From the INTERNATIONAL BUREAU

NOTIFICATION CONCERNING  
SUBMISSION OR TRANSMITTAL  
OF PRIORITY DOCUMENT

(PCT Administrative Instructions, Section 411)

To:

HALLYBONE, Huw, George  
Carpmaels & Ransford  
43 Bloomsbury Square  
London WC1A 2RA  
ROYAUME-UNI

Date of mailing (day/month/year) 11 April 2000 (11.04.00)	IMPORTANT NOTIFICATION
Applicant's or agent's file reference P020968WO	
International application No. PCT/IB00/00219	International filing date (day/month/year) 22 February 2000 (22.02.00)
International publication date (day/month/year) Not yet published	Priority date (day/month/year) 22 February 1999 (22.02.99)
Applicant EUROPEAN MOLECULAR BIOLOGY LABORATORY et al	

- The applicant is hereby notified of the date of receipt (except where the letters "NR" appear in the right-hand column) by the International Bureau of the priority document(s) relating to the earlier application(s) indicated below. Unless otherwise indicated by an asterisk appearing next to a date of receipt, or by the letters "NR", in the right-hand column, the priority document concerned was submitted or transmitted to the International Bureau in compliance with Rule 17.1(a) or (b).
- This updates and replaces any previously issued notification concerning submission or transmittal of priority documents.
- An asterisk(\*) appearing next to a date of receipt, in the right-hand column, denotes a priority document submitted or transmitted to the International Bureau but not in compliance with Rule 17.1(a) or (b). In such a case, the attention of the applicant is directed to Rule 17.1(c) which provides that no designated Office may disregard the priority claim concerned before giving the applicant an opportunity, upon entry into the national phase, to furnish the priority document within a time limit which is reasonable under the circumstances.
- The letters "NR" appearing in the right-hand column denote a priority document which was not received by the International Bureau or which the applicant did not request the receiving Office to prepare and transmit to the International Bureau, as provided by Rule 17.1(a) or (b), respectively. In such a case, the attention of the applicant is directed to Rule 17.1(c) which provides that no designated Office may disregard the priority claim concerned before giving the applicant an opportunity, upon entry into the national phase, to furnish the priority document within a time limit which is reasonable under the circumstances.

<u>Priority date</u>	<u>Priority application No.</u>	<u>Country or regional Office or PCT receiving Office</u>	<u>Date of receipt of priority document</u>
22 Febr 1999 (22.02.99)	9904004.0	GB	22 Marc 2000 (22.03.00)
16 Augu 1999 (16.08.99)	9919369.0	GB	22 Marc 2000 (22.03.00)

The International Bureau of WIPO  
34, chemin des Colombettes  
1211 Geneva 20, Switzerland

Facsimile No. (41-22) 740.14.35

Authorized officer

Marc Salzman

Telephone No. (41-22) 338.83.38

00322156

1257K  
2. HGH

From the INTERNATIONAL BUREAU

PCT

NOTICE INFORMING THE APPLICANT OF THE  
COMMUNICATION OF THE INTERNATIONAL  
APPLICATION TO THE DESIGNATED OFFICES

(PCT Rule 47.1(c), first sentence)

To:

HALLYBONE, Huw, George  
Carpmaels & Ransford  
43 Bloomsbury Square  
London WC1A 2RA  
ROYAUME-UNI

mms

Date of mailing (day/month/year)

31 August 2000 (31.08.00)

Applicant's or agent's file reference

P020968WO

## IMPORTANT NOTICE

International application No.

PCT/IB00/00219

International filing date (day/month/year)

22 February 2000 (22.02.00)

Priority date (day/month/year)

22 February 1999 (22.02.99)

Applicant

EUROPEAN MOLECULAR BIOLOGY LABORATORY et al

1. Notice is hereby given that the International Bureau has communicated, as provided in Article 20, the international application to the following designated Offices on the date indicated above as the date of mailing of this Notice:

AU,KP,KR,US

In accordance with Rule 47.1(c), third sentence, those Offices will accept the present Notice as conclusive evidence that the communication of the international application has duly taken place on the date of mailing indicated above and no copy of the international application is required to be furnished by the applicant to the designated Office(s).

2. The following designated Offices have waived the requirement for such a communication at this time:

AE,AL,AM,AP,AT,AZ,BA,BB,BG,BR,BY,CA,CH,CN,CR,CU,CZ,DE,DK,DM,EA,EE,EP,ES,FI,GB,GD,  
GE,GH,GM,HR,HU,ID,IL,IN,IS,JP,KE,KG,KZ,LC,LK,LR,LS,LT,LU,LV,MA,MD,MG,MK,MN,MW,MX,  
NO,NZ,OA,PL,PT,RO,RU,SD,SE,SG,SI,SK,SL,TJ,TM,TR,TT,TZ,UA,UG,UZ,VN,YU,ZA,ZW

The communication will be made to those Offices only upon their request. Furthermore, those Offices do not require the applicant to furnish a copy of the international application (Rule 49.1(a-bis)).

3. Enclosed with this Notice is a copy of the international application as published by the International Bureau on  
31 August 2000 (31.08.00) under No. WO 00/50586

## REMINDER REGARDING CHAPTER II (Article 31(2)(a) and Rule 54.2)

If the applicant wishes to postpone entry into the national phase until 30 months (or later in some Offices) from the priority date, a demand for international preliminary examination must be filed with the competent International Preliminary Examining Authority before the expiration of 19 months from the priority date.

It is the applicant's sole responsibility to monitor the 19-month time limit.

Note that only an applicant who is a national or resident of a PCT Contracting State which is bound by Chapter II has the right to file a demand for international preliminary examination.

## REMINDER REGARDING ENTRY INTO THE NATIONAL PHASE (Article 22 or 39(1))

If the applicant wishes to proceed with the international application in the national phase, he must, within 20 months or 30 months, or later in some Offices, perform the acts referred to therein before each designated or elected Office.

For further important information on the time limits and acts to be performed for entering the national phase, see the Annex to Form PCT/IB/301 (Notification of Receipt of Record Copy) and Volume II of the PCT Applicant's Guide.

The International Bureau of WIPO  
34, chemin des Colombettes  
1211 Geneva 20, Switzerland

Facsimile No. (41-22) 740.14.35

Authorized officer

J. Zahra

Telephone No. (41-22) 338.83.38

# PCT

## REQUEST

The undersigned requests that the present international application be processed according to the Patent Cooperation Treaty.

For receiving Office use only

International Application No.

International Filing Date

Name of receiving Office and "PCT International Application"

Applicant's or agent's file reference  
(if desired) (12 characters maximum) P020968WO

### Box No. I TITLE OF INVENTION

TRANSLATION SYSTEM

### Box No. II APPLICANT

Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)

EUROPEAN MOLECULAR BIOLOGY LABORATORY  
P.O. Box 10 22 09  
Meyerhofstr. 1  
69012 Heidelberg  
GERMANY

☐ This person is also inventor.

Telephone No.

Facsimile No.

Teleprinter No.

State (that is, country) of nationality:

DE

State (that is, country) of residence:

DE

This person is applicant for the purposes of:

☐ all designated States

☒ all designated States except the United States of America

☐ the United States of America only

☐ the States indicated in the Supplemental Box

### Box No. III FURTHER APPLICANT(S) AND/OR (FURTHER) INVENTOR(S)

Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)

GEBAUER, Fatima  
Lerchenstrasse 28  
69251 Gaiberg  
GERMANY

This person is:

☐ applicant only

☒ applicant and inventor

☐ inventor only (If this check-box is marked, do not fill in below.)

State (that is, country) of nationality:

ES

State (that is, country) of residence:

DE

This person is applicant for the purposes of:

☐ all designated States

☐ all designated States except the United States of America

☒ the United States of America only

☐ the States indicated in the Supplemental Box

☒ Further applicants and/or (further) inventors are indicated on a continuation sheet.

### Box No. IV AGENT OR COMMON REPRESENTATIVE; OR ADDRESS FOR CORRESPONDENCE

The person identified below is hereby/has been appointed to act on behalf of the applicant(s) before the competent International Authorities as:

☒ agent

☐ common representative

Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country.)

HALLYBONE, Huw George  
CARPMAELS & RANSFORD  
43 BLOOMSBURY SQUARE  
LONDON WC1A 2RA  
GB

Telephone No.

+44 20-7242 8692

Facsimile No.

+44 20-7405 4166

Teleprinter No.

267209

☐ Address for correspondence: Mark this check-box where no agent or common representative is/has been appointed and the space above is used instead to indicate a special address to which correspondence should be sent.



## Continuation of Box No. III FURTHER APPLICANT(S) AND/OR (FURTHER) INVENTOR(S)

If none of the following sub-boxes is used, this sheet should not be included in the request

Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)

CORONA, Davide  
Brechtelstrasse 8-10  
69126 Heidelberg  
GERMANY

This person is:

- ☐ applicant only
- ☒ applicant and inventor
- ☐ inventor only (If this check-box is marked, do not fill in below.)

State (that is, country) of nationality:  
IT

State (that is, country) of residence:  
DE

This person is applicant  
for the purposes of:

- ☐ all designated States ☐ all designated States except the United States of America ☒ the United States of America only ☐ the States indicated in the Supplemental Box

Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)

BERGAMINI, Giovanna  
Römerstr. 25  
69115 Heidelberg  
GERMANY

This person is:

- ☐ applicant only
- ☒ applicant and inventor
- ☐ inventor only (If this check-box is marked, do not fill in below.)

State (that is, country) of nationality:  
IT

State (that is, country) of residence:  
DE

This person is applicant  
for the purposes of:

- ☐ all designated States ☐ all designated States except the United States of America ☒ the United States of America only ☐ the States indicated in the Supplemental Box

Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)

BECKER, Peter  
Salzstr. 9  
82194 Gröbenzell  
GERMANY

This person is:

- ☐ applicant only
- ☒ applicant and inventor
- ☐ inventor only (If this check-box is marked, do not fill in below.)

State (that is, country) of nationality:  
DE

State (that is, country) of residence:  
DE

This person is applicant  
for the purposes of:

- ☐ all designated States ☐ all designated States except the United States of America ☒ the United States of America only ☐ the States indicated in the Supplemental Box

Name and address: (Family name followed by given name; for a legal entity, full official designation. The address must include postal code and name of country. The country of the address indicated in this Box is the applicant's State (that is, country) of residence if no State of residence is indicated below.)

HENTZE, Matthias  
Merianstr. 5  
69117 Heidelberg  
GERMANY

This person is:

- ☐ applicant only
- ☒ applicant and inventor
- ☐ inventor only (If this check-box is marked, do not fill in below.)

State (that is, country) of nationality:  
DE

State (that is, country) of residence:  
DE

This person is applicant  
for the purposes of:

- ☐ all designated States ☐ all designated States except the United States of America ☒ the United States of America only ☐ the States indicated in the Supplemental Box

☐ Further applicants and/or (further) inventors are indicated on another continuation sheet.

**Box No.V DESIGNATION OF STATES**

The following designations are hereby made under Rule 4.9(a) (mark the applicable check-boxes; at least one must be marked):

**Regional Patent**

- ☒ **AP** ARIPO Patent: GH Ghana, GM Gambia, KE Kenya, LS Lesotho, MW Malawi, SD Sudan, SL Sierra Leone, SZ Swaziland, TZ United Republic of Tanzania, UG Uganda, ZW Zimbabwe, and any other State which is a Contracting State of the Harare Protocol and of the PCT
- ☒ **EA** Eurasian Patent: AM Armenia, AZ Azerbaijan, BY Belarus, KG Kyrgyzstan, KZ Kazakhstan, MD Republic of Moldova, RU Russian Federation, TJ Tajikistan, TM Turkmenistan, and any other State which is a Contracting State of the Eurasian Patent Convention and of the PCT
- ☒ **EP** European Patent: AT Austria, BE Belgium, CH and LI Switzerland and Liechtenstein, CY Cyprus, DE Germany, DK Denmark, ES Spain, FI Finland, FR France, GB United Kingdom, GR Greece, IE Ireland, IT Italy, LU Luxembourg, MC Monaco, NL Netherlands, PT Portugal, SE Sweden, and any other State which is a Contracting State of the European Patent Convention and of the PCT
- ☒ **OA** OAPI Patent: BF Burkina Faso, BJ Benin, CF Central African Republic, CG Congo, CI Côte d'Ivoire, CM Cameroon, GA Gabon, GN Guinea, GW Guinea-Bissau, ML Mali, MR Mauritania, NE Niger, SN Senegal, TD Chad, TG Togo, and any other State which is a member State of OAPI and a Contracting State of the PCT (if other kind of protection or treatment desired, specify on dotted line)

**National Patent (if other kind of protection or treatment desired, specify on dotted line):**

- |   |   |
|---|---|
| <input checked="" type="checkbox"/> <b>AE</b> United Arab Emirates                  | <input checked="" type="checkbox"/> <b>LR</b> Liberia                                   |
| <input checked="" type="checkbox"/> <b>AL</b> Albania                               | <input checked="" type="checkbox"/> <b>LS</b> Lesotho                                   |
| <input checked="" type="checkbox"/> <b>AM</b> Armenia                               | <input checked="" type="checkbox"/> <b>LT</b> Lithuania                                 |
| <input checked="" type="checkbox"/> <b>AT</b> Austria                               | <input checked="" type="checkbox"/> <b>LU</b> Luxembourg                                |
| <input checked="" type="checkbox"/> <b>AU</b> Australia                             | <input checked="" type="checkbox"/> <b>LV</b> Latvia                                    |
| <input checked="" type="checkbox"/> <b>AZ</b> Azerbaijan                            | <input checked="" type="checkbox"/> <b>MA</b> Morocco                                   |
| <input checked="" type="checkbox"/> <b>BA</b> Bosnia and Herzegovina                | <input checked="" type="checkbox"/> <b>MD</b> Republic of Moldova                       |
| <input checked="" type="checkbox"/> <b>BB</b> Barbados                              | <input checked="" type="checkbox"/> <b>MG</b> Madagascar                                |
| <input checked="" type="checkbox"/> <b>BG</b> Bulgaria                              | <input checked="" type="checkbox"/> <b>MK</b> The former Yugoslav Republic of Macedonia |
| <input checked="" type="checkbox"/> <b>BR</b> Brazil                                |   |
| <input checked="" type="checkbox"/> <b>BY</b> Belarus                               | <input checked="" type="checkbox"/> <b>MN</b> Mongolia                                  |
| <input checked="" type="checkbox"/> <b>CA</b> Canada                                | <input checked="" type="checkbox"/> <b>MW</b> Malawi                                    |
| <input checked="" type="checkbox"/> <b>CH and LI</b> Switzerland and Liechtenstein  | <input checked="" type="checkbox"/> <b>MX</b> Mexico                                    |
| <input checked="" type="checkbox"/> <b>CN</b> China                                 | <input checked="" type="checkbox"/> <b>NO</b> Norway                                    |
| <input checked="" type="checkbox"/> <b>CR</b> Costa Rica                            | <input checked="" type="checkbox"/> <b>NZ</b> New Zealand                               |
| <input checked="" type="checkbox"/> <b>CU</b> Cuba                                  | <input checked="" type="checkbox"/> <b>PL</b> Poland                                    |
| <input checked="" type="checkbox"/> <b>CZ</b> Czech Republic                        | <input checked="" type="checkbox"/> <b>PT</b> Portugal                                  |
| <input checked="" type="checkbox"/> <b>DE</b> Germany                               | <input checked="" type="checkbox"/> <b>RO</b> Romania                                   |
| <input checked="" type="checkbox"/> <b>DK</b> Denmark                               | <input checked="" type="checkbox"/> <b>RU</b> Russian Federation                        |
| <input checked="" type="checkbox"/> <b>DM</b> Dominica                              | <input checked="" type="checkbox"/> <b>SD</b> Sudan                                     |
| <input checked="" type="checkbox"/> <b>EE</b> Estonia                               | <input checked="" type="checkbox"/> <b>SE</b> Sweden                                    |
| <input checked="" type="checkbox"/> <b>ES</b> Spain                                 | <input checked="" type="checkbox"/> <b>SG</b> Singapore                                 |
| <input checked="" type="checkbox"/> <b>FI</b> Finland                               | <input checked="" type="checkbox"/> <b>SI</b> Slovenia                                  |
| <input checked="" type="checkbox"/> <b>GB</b> United Kingdom                        | <input checked="" type="checkbox"/> <b>SK</b> Slovakia                                  |
| <input checked="" type="checkbox"/> <b>GD</b> Grenada                               | <input checked="" type="checkbox"/> <b>SL</b> Sierra Leone                              |
| <input checked="" type="checkbox"/> <b>GE</b> Georgia                               | <input checked="" type="checkbox"/> <b>TJ</b> Tajikistan                                |
| <input checked="" type="checkbox"/> <b>GH</b> Ghana                                 | <input checked="" type="checkbox"/> <b>TM</b> Turkmenistan                              |
| <input checked="" type="checkbox"/> <b>GM</b> Gambia                                | <input checked="" type="checkbox"/> <b>TR</b> Turkey                                    |
| <input checked="" type="checkbox"/> <b>HR</b> Croatia                               | <input checked="" type="checkbox"/> <b>TT</b> Trinidad and Tobago                       |
| <input checked="" type="checkbox"/> <b>HU</b> Hungary                               | <input checked="" type="checkbox"/> <b>TZ</b> United Republic of Tanzania               |
| <input checked="" type="checkbox"/> <b>ID</b> Indonesia                             | <input checked="" type="checkbox"/> <b>UA</b> Ukraine                                   |
| <input checked="" type="checkbox"/> <b>IL</b> Israel                                | <input checked="" type="checkbox"/> <b>UG</b> Uganda                                    |
| <input checked="" type="checkbox"/> <b>IN</b> India                                 | <input checked="" type="checkbox"/> <b>US</b> United States of America                  |
| <input checked="" type="checkbox"/> <b>IS</b> Iceland                               |   |
| <input checked="" type="checkbox"/> <b>JP</b> Japan                                 | <input checked="" type="checkbox"/> <b>UZ</b> Uzbekistan                                |
| <input checked="" type="checkbox"/> <b>KE</b> Kenya                                 | <input checked="" type="checkbox"/> <b>VN</b> Viet Nam                                  |
| <input checked="" type="checkbox"/> <b>KG</b> Kyrgyzstan                            | <input checked="" type="checkbox"/> <b>YU</b> Yugoslavia                                |
| <input checked="" type="checkbox"/> <b>KP</b> Democratic People's Republic of Korea | <input checked="" type="checkbox"/> <b>ZA</b> South Africa                              |
|   | <input checked="" type="checkbox"/> <b>ZW</b> Zimbabwe                                  |
- Check-boxes reserved for designating States which have become party to the PCT after issuance of this sheet:
- ☐ .....
- ☐ .....

**Precautionary Designation Statement:** In addition to the designations made above, the applicant also makes under Rule 4.9(b) all other designations which would be permitted under the PCT except any designation(s) indicated in the Supplemental Box as being excluded from the scope of this statement. The applicant declares that those additional designations are subject to confirmation and that any designation which is not confirmed before the expiration of 15 months from the priority date is to be regarded as withdrawn by the applicant at the expiration of that time limit. (Confirmation (including fees) must reach the receiving Office within the 15-month time limit.)

## Box No. VI PRIORITY CLAIM

☐ Further priority claims are indicated in the Supplemental Box.

Filing date of earlier application (day/month/year)	Number of earlier application	Where earlier application is:		
		national application: country	regional application: <sup>*</sup> regional Office	international application: receiving Office
item (1) 22 Feb 99 (22/2/99)	9904004.0	GB		
item (2) 16 Aug 99 (16/8/99)	9919369.0	GB		
item (3)				

☒ The receiving Office is requested to prepare and transmit to the International Bureau a certified copy of the earlier application(s) (only if the earlier application was filed with the Office which for the purposes of the present international application is the receiving Office) identified above as item(s): (2) GB 9919369.0 (1) GB 9904004.0

<sup>\*</sup> Where the earlier application is an ARIPO application, it is mandatory to indicate in the Supplemental Box at least one country party to the Paris Convention for the Protection of Industrial Property for which that earlier application was filed (Rule 4.10(b)(ii)). See Supplemental Box.

## Box No. VII INTERNATIONAL SEARCHING AUTHORITY

Choice of International Searching Authority (ISA) (if two or more International Searching Authorities are competent to carry out the international search, indicate the Authority chosen; the two-letter code may be used):

ISA / EP

Request to use results of earlier search; reference to that search (if an earlier search has been carried out by or requested from the International Searching Authority):

Date (day/month/year)

Number

Country (or regional Office)

## Box No. VIII CHECK LIST; LANGUAGE OF FILING

This international application contains the following number of sheets:

request : 4

description (excluding sequence listing part) : 22

claims : 6

abstract : 1

drawings : 13

sequence listing part of description :

Total number of sheets : 46

This international application is accompanied by the item(s) marked below:

1. ☒ fee calculation sheet
2. ☐ separate signed power of attorney
3. ☐ copy of general power of attorney; reference number, if any:
4. ☐ statement explaining lack of signature
5. ☐ priority document(s) identified in Box No. VI as item(s):
6. ☐ translation of international application into (language):
7. ☐ separate indications concerning deposited microorganism or other biological material
8. ☐ nucleotide and/or amino acid sequence listing in computer readable form
9. ☒ other (specify): 23/77

Figure of the drawings which should accompany the abstract:

Language of filing of the international application: ENGLISH

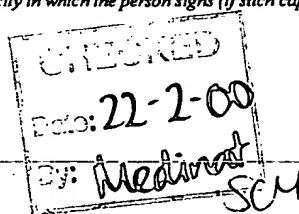
## Box No. IX SIGNATURE OF APPLICANT OR AGENT

Next to each signature, indicate the name of the person signing and the capacity in which the person signs (if such capacity is not obvious from reading the request).

P. J. Howard

HOWARD, Paul Nicholas

for HALLYBONE, Huw George



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1. Date of actual receipt of the purported international application:	2. Drawings:  <input type="checkbox"/> received:  <input type="checkbox"/> not received:
3. Corrected date of actual receipt due to later but timely received papers or drawings completing the purported international application:	
4. Date of timely receipt of the required corrections under PCT Article 11(2):	
5. International Searching Authority (if two or more are competent): ISA /	6. <input type="checkbox"/> Transmittal of search copy delayed until search fee is paid.

For International Bureau use only

Date of receipt of the record copy by the International Bureau:

(19) World Intellectual Property Organization  
International Bureau(43) International Publication Date  
31 August 2000 (31.08.2000)

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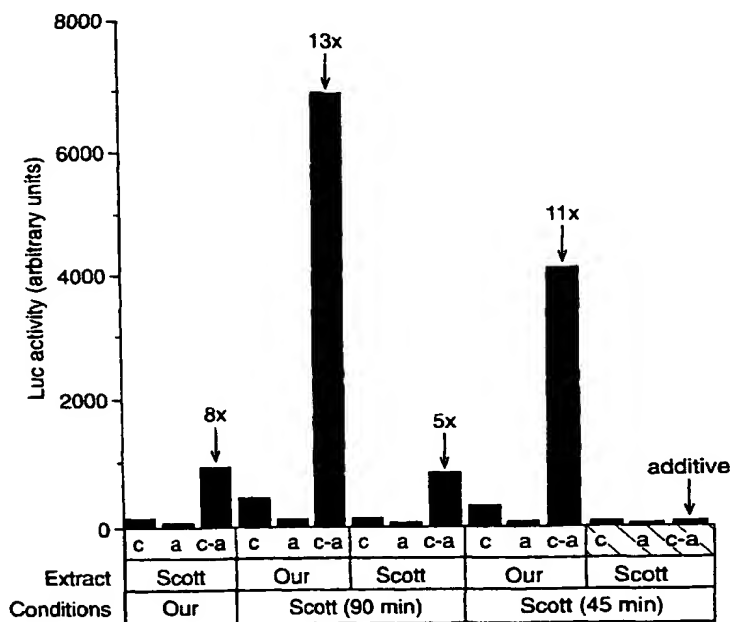
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[Continued on next page]

(54) Title: IN VITRO TRANSLATION SYSTEM

Experiment E-872 Blow up (one set of data eliminated)  
c = cap, a = poly(A), c-a = cap and poly(A)  
Synergism = fold over the sum of c+a value



(57) Abstract: The invention relates to a cell-free translation system using cell extracts, that reproduces the synergism that occurs during translation *in vivo* between the cap and the poly(A) tail structures of an mRNA molecule. Using this system, the amount of encoded protein produced from translation of an mRNA molecule is greater than the total of (a) the amount of the encoded protein that is produced under the same conditions when the ribonucleic acid template has a 5' cap but no 3' poly A tail, plus (b) the amount of the encoded protein that is produced under the same conditions when the ribonucleic acid template has a 3' poly A tail but no 5' cap.

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